



## Complete Summary

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### GUIDELINE TITLE

Case detection, diagnosis, and treatment of patients with primary aldosteronism: an Endocrine Society clinical practice guideline.

### BIBLIOGRAPHIC SOURCE(S)

Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M, Young WF Jr, Montori VM, Endocrine Society. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2008 Sep;93(9):3266-81. [139 references] [PubMed](#)

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Primary aldosteronism

### GUIDELINE CATEGORY

Diagnosis  
Screening  
Treatment

### CLINICAL SPECIALTY

Cardiology  
Endocrinology  
Internal Medicine  
Medical Genetics  
Radiology  
Surgery

## **INTENDED USERS**

Physicians

## **GUIDELINE OBJECTIVE(S)**

To provide clinical practice guidelines for the diagnosis and treatment of patients with primary aldosteronism

## **TARGET POPULATION**

- Patients with clinical features suggestive of primary aldosteronism (PA), including:
  - Patients with stage 2 (>160 to 179/100 to 109 mm Hg), stage 3 (>180/110 mm Hg), or drug resistant hypertension
  - Patients with hypertension and spontaneous or diuretic-induced hypokalemia
  - Patients with hypertension with adrenal incidentaloma
  - Patients with hypertension and a family history of early-onset hypertension or cerebrovascular accident at a young age (<40 years)
  - Patients with hypertension and a first-degree relative with PA
- Patients with confirmed PA

## **INTERVENTIONS AND PRACTICES CONSIDERED**

### **Diagnosis**

1. Case detection based on clinical characteristics and family history
2. Plasma aldosterone-renin ratio (ARR) for initial testing
3. Confirmatory testing
  - Oral sodium loading
  - Saline infusion
  - Fludrocortisone suppression
  - Captopril challenge
4. Adrenal computed tomography (CT) scan for subtype testing
5. Adrenal venous sampling (AVS) to distinguish between unilateral and bilateral adrenal disease
6. Genetic testing for glucocorticoid-remediable aldosteronism (GRA)

### **Treatment**

1. Unilateral laparoscopic adrenalectomy
2. Mineralocorticoid receptor (MR) antagonist
  - Spironolactone

- Eplerenone
3. Glucocorticoid

## MAJOR OUTCOMES CONSIDERED

- Sensitivity, specificity, reliability, and accuracy of diagnostic tests
- Response to treatment (blood pressure control, normalization of endogenous aldosterone secretion, resolution of hypokalemia)
- Side effects of treatment

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

#### Quality of the Evidence

**+000** Denotes very low quality evidence

**++00** Denotes low quality evidence

**+++0** Denotes moderate quality evidence

**++++** Denotes high quality evidence

### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

### **Participants**

The Task Force comprised a chair, selected by the Clinical Guidelines Subcommittee (CGS) of The Endocrine Society, six additional experts, one methodologist, and a medical writer.

### **Evidence**

Systematic reviews of available evidence were used to formulate the key treatment and prevention recommendations. The authors used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group criteria to describe both the quality of evidence and the strength of recommendations. The authors used 'recommend' for strong recommendations and 'suggest' for weak recommendations.

### **Consensus Process**

Consensus was guided by systematic reviews of evidence and discussions during one group meeting, several conference calls, and multiple e-mail communications. The drafts were then prepared by the Task Force with the help of a medical writer.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

### **Strength of Recommendations**

- The number 1 indicates a strong recommendation and is associated with the phrase "The Task Force recommends."
- The number 2 denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

## **COST ANALYSIS**

One published study has shown that, in the long term, adrenalectomy is more cost-effective than lifelong medical therapy for patients with unilateral primary aldosteronism.

## **METHOD OF GUIDELINE VALIDATION**

External Peer Review  
Internal Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

The drafts were reviewed by The Endocrine Society's Clinical Guideline Subcommittee (CGS), Clinical Affairs Core Committee (CACC), and Council. The version approved by the CGS and CACC was placed on The Endocrine Society's Web site for comments by members. At each stage of review, the Task Force received written comments and incorporated needed changes.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Definitions for the quality of the evidence (+OOO, ++OO, +++O, and ++++); the strength of the recommendation (1 or 2); and for the difference between a "recommendation" and a "suggestion" are provided at the end of the "Major Recommendations" field.

#### Case Detection

The Task Force recommends the case detection of primary aldosteronism (PA) in patient groups with relatively high prevalence of PA. (1 | ++OO) These include patients with Joint National Commission (JNC) stage 2 (>160/179/100–109 mm Hg), stage 3 (>180/110 mm Hg), or drug resistant hypertension; hypertension and spontaneous or diuretic-induced hypokalemia; hypertension with adrenal incidentaloma; or hypertension and a family history of early onset hypertension or cerebrovascular accident at a young age (<40 years). The Task Force also recommends case detection for all hypertensive first-degree relatives of patients with PA. (1 | +OOO)

The Task Force recommends use of the plasma aldosterone-renin ratio (ARR) to detect cases of PA in these patient groups. (1 | ++OO)

#### Case Confirmation

Instead of proceeding directly to subtype classification, the Task Force recommends that patients with a positive aldosterone-renin ratio (ARR) undergo testing, by any of four confirmatory tests, to definitively confirm or exclude the diagnosis. (1 | ++OO)

#### Subtype Classification

The Task Force recommends that all patients with PA undergo an adrenal computed tomography (CT) scan as the initial study in subtype testing and to exclude large masses that may represent adrenocortical carcinoma. (1 | ++OO)

The Task Force recommends that, when surgical treatment is practicable and desired by the patient, the distinction between unilateral and bilateral adrenal disease be made by adrenal venous sampling (AVS) by an experienced radiologist. (1 | +++O)

In patients with onset of confirmed PA earlier than at 20 years of age and in those who have a family history of PA or of strokes at young age (<40 years), the Task

Force suggests genetic testing for glucocorticoid-remediable aldosteronism (GRA). (2 | +000)

## **Treatment**

The Task Force recommends that treatment by unilateral laparoscopic adrenalectomy be offered to patients with documented unilateral PA (i.e., aldosterone-producing adenoma [APA] or unilateral adrenal hyperplasia [UAH]). (1 | ++00) If a patient is unable or unwilling to undergo surgery, the Task Force recommends medical treatment with a mineralocorticoid receptor (MR) antagonist. (1 | ++00)

In patients with PA due to bilateral adrenal disease, the Task Force recommends medical treatment with an MR antagonist (1 | ++00); the Task Force suggests spironolactone as the primary agent with eplerenone as an alternative. (2 | +000)

In patients with GRA, the Task Force recommends the use of the lowest dose of glucocorticoid that can normalize blood pressure and serum potassium levels rather than first-line treatment with a mineralocorticoid receptor (MR) antagonist. (1 | +000)

## **Definitions:**

### **Strength of Recommendations**

**1** - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

**2** - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

### **Quality of the Evidence**

**+000** Denotes very low quality evidence

**++00** Denotes low quality evidence

**+++0** Denotes moderate quality evidence

**++++** Denotes high quality evidence

### **CLINICAL ALGORITHM(S)**

An algorithm for the detection, confirmation, subtype testing, and treatment of primary aldosteronism is provided in the original guideline document under Figure 1.

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

In the original guideline document, each *recommendation* is linked to a description of the *evidence*, *values* that panelists considered in making the recommendation (when making these explicit was necessary), and *remarks*, a section in which panelists offer technical suggestions for testing conditions, dosing, and monitoring. These technical comments reflect the best available evidence applied to a typical patient. Often this evidence comes from the unsystematic observations of the panelists and should therefore be considered suggestions.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Early detection, diagnosis, and treatment of primary aldosteronism may lead to decreased morbidity and mortality and improved quality of life.

### POTENTIAL HARMS

- Confirmatory testing requiring oral or intravenous sodium loading should be administered with caution in patients with uncontrolled hypertension or congestive heart failure.
- Medications, potassium status, dietary sodium, advancing age, and other conditions may affect the aldosterone-renin ratio and thus lead to false-positive or false-negative results (see Table 4 of the original guideline document for a list of factors).
- Computed tomography (CT) has the potential to be misleading by demonstrating unilateral nodules in patients with bilateral disease and thereby to lead to inappropriate surgery.
- Potential side effects from use of mineralocorticoid receptor (MR) antagonists and glucocorticoids
- Risks of surgery
- Patients could potentially be harmed by the work up and treatment (i.e., by withdrawal of antihypertensive medication, invasive vascular examination, adrenalectomy) aimed at vascular protection along with easier and better blood pressure control.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- Clinical Practice Guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all

proper approaches or methods, or exclusive of others. The guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of health care providers and each patient's individual circumstances.

- The Endocrine Society makes no warranty, express or implied, regarding the Guidelines and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The Society shall not be liable for direct, indirect, special, incidental, or consequential damages related to the use of the information contained herein.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

### IMPLEMENTATION TOOLS

Clinical Algorithm  
Foreign Language Translations  
Patient Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness  
Staying Healthy

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M, Young WF Jr, Montori VM, Endocrine Society. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2008 Sep;93(9):3266-81. [139 references] [PubMed](#)

**ADAPTATION**

Not applicable: The guideline was not adapted from another source.

**DATE RELEASED**

2008 Sep

**GUIDELINE DEVELOPER(S)**

The Endocrine Society - Disease Specific Society

**SOURCE(S) OF FUNDING**

The Endocrine Society

**GUIDELINE COMMITTEE**

Case Detection, Diagnosis, and Treatment of Patients with Primary Aldosteronism Task Force

**COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

*Task Force Members:* John W. Funder; Robert M. Carey; Carlos Fardella; Celso E. Gomez-Sanchez; Franco Mantero; Michael Stowasser; William F. Young Jr; Victor M. Montori

**FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

John W. Funder, MD, PhD (*Chair*)—Financial or Business/Organizational Interests: Schering-Plough, Daiichi-Sankyo, Pfizer, Cancer Institute of N.S.W, Speedel, Garnett Passe and Rodney Williams Memorial Foundation, Merck, Eli Lilly, P3 Panel (Commonwealth of Australia); Significant Financial Interest or Leadership Position: Schering-Plough, Pfizer, Daiichi-Sankyo and Cancer Institute of N.S.W.

Robert M. Carey, MD—Financial or Business/Organizational Interests: Novartis, Pfizer, Daiichi-Sankyo; Significant Financial Interest or Leadership Position: none declared.

Carlos Fardella, MD—Financial or Business/Organizational Interests: National Fund for Scientific and Technological Development (Fondo Nacional de Desarrollo Científico y Tecnológico [FONDECYT]); Significant Financial Interest or Leadership Position: none declared.

Celso E. Gomez-Sanchez, MD—Financial or Business/Organizational Interests: American Heart Association; Significant Financial Interest or Leadership Position: Associate Editor for the journal Hypertension.

Franco Mantero, MD, PhD—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: Executive Committee of the International Society of Endocrinology.

Michael Stowasser, MBBS, FRACP, PhD—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: none declared.

William F. Young Jr., MSc, MD—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: Mayo Clinic, Clinical Endocrinology.

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*\*Evidence-based reviews for this guideline were prepared under contract with The Endocrine Society.*

## **ENDORSER(S)**

European Society of Endocrinology - Medical Specialty Society  
European Society of Hypertension - Disease Specific Society  
International Society of Endocrinology - Medical Specialty Society  
International Society of Hypertension - Disease Specific Society  
Japanese Society of Hypertension - Disease Specific Society

## **GUIDELINE STATUS**

This is the current release of the guideline.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available in Portable Document Format (PDF) from [The Endocrine Society](#).

Print copies: Available from The Endocrine Society, c/o Bank of America, P.O. Box 630721, Baltimore, MD 21263-0736; Phone: (301) 941.0210; Email: [SocietyServices@endo-society.org](mailto:SocietyServices@endo-society.org)

## **AVAILABILITY OF COMPANION DOCUMENTS**

None available

## **PATIENT RESOURCES**

The following are available:

- The Hormone Foundation's patient guide to detection, diagnosis and treatment of primary aldosteronism. Chevy Chase (MD): The Hormone Foundation. 2008 Sep. 2 p. Available from the [Hormone Foundation Web site](#).

- The Hormone Foundation's patient fact sheet: primary aldosteronism. Chevy Chase (MD): The Hormone Foundation. 2007 Dec. 1 p. Available in English and Spanish from the [Hormone Foundation Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## **NGC STATUS**

This NGC summary was completed by ECRI Institute on January 15, 2009. The information was verified by the guideline developer on February 4, 2009.

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